The Harveian Lectures
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ROBERT MAGUIRE

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ON

PROGNOSIS AND TREATMENT

IN

PULMONARY TUBERCULOSIS

Delivered before the Harveian Society of London on November 1st, 8th, and 15th, 1900,

BY

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ON

PROGNOSIS AND TREATMENT IN PULMONARY TUBERCULOSIS.

LECTURE I.

Delivered on Nov. 1st, 1900.

MR. PRESIDENT AND GENTLEMEN,—I thank you heartily for the honour you have done me in asking me to deliver your annual Harveian Lectures. In choosing a subject for them I could not but be influenced by the methods used by the man whose name you have chosen to designate this society and these lectures. He trusted especially to observation and made theory subservient to this. Bacon's maxim of "Hypotheses non fingo" is said to be wrong, and taken literally no doubt is wrong. Newton, finding, as it is said, his facts after his theories, did good work and his method has been followed by some in our profession with success, but only by few. Yet Newton first saw the apple fall before he reasoned from that fact, and therein he followed the Baconian method. Again, let us remember that Newton dealt with very simple sciences—only with astronomy, physics, and chemistry—nature in its normality, however complex that normality may be, and from normalities one may comparatively easily be led to certainties, as, indeed, Newton was. We, on the other hand, have to deal with nature in its abnormality, a vastly more complex science, in which theories must be outside our knowledge until facts—much more indefinite than the fall of Newton's apple—are carefully observed. Let us start then by recording our facts in the way Bacon did, in which Newton actually did, though he is said to have pursued another process in his reasoning, and in which Harvey combined the methods of both. Let us only very carefully suggest theories after facts have been well observed and try not to go beyond those facts.

I wish to present to you facts and then conclusions from those facts. Therefore I have chosen a subject upon which I can deal with facts from a somewhat large experience, and can give you the conclusions which I myself have been able to draw from them. Thus I have taken as my subject, Prognosis and Treatment in Pulmonary Tuberculosis, and yet let me at once say that I do not intend to deal with the whole of that subject. To do so would lead me beyond our three lectures and would cause me to tell you many things which you know already, and others which you can just as well read in the text-books or in the journals as you can learn from me. I wish only to give you points which I have learnt myself from experience and to ignore, as far as possible, those which I have learnt from others, as you also can learn them from others. I appeal for my facts especially to the records of the large number of patients intrusted to my care at the Brompton Hospital for Consumption and Diseases of the Chest, in the out-patient department, later to those of the in-patient department, and to others seen elsewhere. Again, I have made use of the records of the post-mortem rooms at the Brompton Hospital, at St. Mary's Hospital, and at the Manchester Royal Infirmary during the periods in which I was pathologist to those several institutions, while, finally, I will give you facts from experiments on animals and upon myself, mainly relating to a new method of treatment of pulmonary tuberculosis, which will be described in my third lecture. There I will describe how I have taken advantage of Harvey's great discovery, the circulation of the blood, and, as I hope, for practical advantage in the treatment of disease. Such conclusions as I have been able to draw from the facts I will offer for your consideration, but I intend to make no inferences which the facts cannot reasonably warrant.

Prognosis ought to be based upon full diagnosis, that is, not the mere naming of the disease, but a knowledge of its nature and its course, and a power of appreciating the tendency of such course, and of the signs which indicate its progress. Prognosis sometimes seems to come to a man by instinct, or by what my late and most revered master, Sir William Roberts, used to call "clinical acumen." Some men, and only few, have this power, but even such persons, it has always appeared to me, arrived at their results from unconscious observation and reasoning. They would tell you that a certain course would be pursued by a certain case of disease and that they did not know why they thought so, yet such men have always had keen observation and, unknown to themselves, have reasoned from observed facts. For the majority of us to trust to any such instinct would be fatal to our conclusions, and we ought therefore carefully to reason only from well-observed facts.

Let us, then, apply the method I have mentioned to the prognosis and treatment of pulmonary tuberculosis, under-

standing by this disease, not all the cases which are vulgarly called "phthisis" or "consumption"—though we may by accident occasionally lapse into the use of these terms—but only those affections of the lungs which are accompanied and caused by the presence of the bacillus tuberculosis. And yet let us also remember in estimating our prognosis and in considering our treatment that the tubercle bacillus does not perform its noxious work alone but is aided by at least two other germs, the staphylococcus pyogenes, causing suppuration, and the pneumococcus, causing pneumonia, and each, together with the tubercle bacillus, causing poisoning of the general system by its own scarcely yet recognised product. We must then consider pulmonary tuberculosis, as seen clinically, to be a product of all these three germs, and we must form our prognostic opinion and our therapeutic methods upon observation of the effects which each or all of these germs has produced upon the lungs or upon the general system at any particular time.

We hear occasionally of a pre-bacillary stage of phthisis. This no doubt exists, but with it we have here nothing to do. We have been accustomed also to divide the conditions of pulmonary tuberculosis into three stages, according to their clinical manifestations, and to speak of (1) consolidation, (2) softening, and (3) cavitation—names useful enough in their way, but conveying not much to the mind beyond the condition of physical signs which causes their discovery.

Let us, for the purpose of prognosis, think again of three stages, similar to those already mentioned, but described rather in view of the pathological conditions which we know, or ought to know, are accompanying them, and we may style these stages, in view of the progressive action of the tubercle bacillus and its companions, (1) invasion, (2) progress, and (3) result. In each case we suppose the tubercle bacillus to be the main noxious germ, but, except after the quite early period, to be accompanied by the staphylococcus and pneumococcus. Further, the second stage in one part of a lung may undoubtedly be accompanied by the first stage in another neighbouring or remote part, and the third stage, "result" or destruction of lung-tissue, may be accompanied, similarly, by both the former stages.

Still another factor must be considered in our prognosis and that is the resistance of the lung and general body powers to the invasion of the bacillus—a most important matter, for by it many apparently pneumonic processes may be caused, and these may be not unhealthy but curative—"chemiotaxic," as they are called.

All these points must be considered in forming a prognosis and we must discuss them in certain of their aspects under these several headings.

And yet still something else must be defined before we approach the subject proper, and that is what we ought rightly to understand by prognosis in each of the above stages of

the disease. In the first stage, that of invasion, we wish to attain to complete cure of the patient, an absolute arrest of the bacillary invasion, and a return of the lung to an entirely normal condition, and yet with the same tendency to re-infection which previously existed, a tendency innate in the subject. That tendency having once shown itself, perhaps being recognised for the first time on the outbreak of the lung trouble, may be combated by suitable means, but for a long period must remain hanging over the patient. Such is the most favourable result to which we can attain by the use of all remedies at our disposal, and its probability we style a "favourable prognosis."

When the disease has reached the second stage—that of progress of the bacillary infection—we still hope for arrest of the disease, but if this is to be accomplished it will only be after a certain amount of damage to the lung tissue has been done—damage which is evidenced afterwards by cicatricial tissue and pleural adhesions, and yet damage which eventually may give the patient no trouble if only that other factor (the tendency to further attacks) be kept well under control. Thus the most favourable result to be obtained in the second stage does not materially differ from that in the first stage.

In the third stage, however, the most favourable prognosis is by no means so good. The "result," as we have chosen to call this stage of bacillary action, is absolute destruction of lung tissue. The active process may be stopped, the progress of destruction may be limited, but the loss of lung tissue can never be made good. Not that this matters greatly, for we all of us have a great deal more lung tissue than we require for the ordinary purposes of life. When I gave up the out-patient department of the Brompton Hospital there was amongst my patients a woman who had attended me for more than seven years and at the hospital for some 15 years. She looked the picture of good health and had continued her attendance more for the sake of being observed than for aught else. I used frequently to ask the gentlemen who attended my clinique to guess her disease from her appearance and they always supposed that she must be one of the dyspeptics of whom, as in all hospital out-patient departments, we had a considerable number. Yet that woman's lungs were riddled with cavities. But a person who has lost any considerable portion of lung tissue is living without respiratory reserve and obviously an accidental bronchitis or pneumonia, such as we are all subject to, will be for him a much more serious matter than for one who has the whole of his lung area intact. Moreover, there are other conditions incident upon the presence of cavities which are dangerous, such as the accumulation and putrefaction of secretions and the formation of pulmonary aneurysms, with others of which more will be said. Thus the most favourable prognosis which we can make in the third stage must be vastly less favourable than that of either of the two

preceding stages. In speaking of "a favourable prognosis" let us therefore consider always the limit to which the healing process can reach in the stage which we have diagnosed. Finally, if actual cure or arrest be beyond the powers of aided or unaided nature we may still estimate the probable rapidity of the disease process and consequently the duration of life and the comfort of the patient during such life as remains to him.

I propose to discuss the influence of all these matters and also of the antecedent conditions, and for convenience we will use the following headings—namely, the influence on prognosis (1) of the nature of the physical signs; (2) of the localisation of the physical signs; (3) of antecedent conditions; and (4) of individual symptoms.

Slight lack of resonance, with deficiency of breath sounds and of respiratory movement but without adventitious sounds, and these signs again limited to one apex, indicate a well-known physical condition, of which, however, we have no accurate post-mortem record. We believe, however, that the condition is one of slight collapse of the air vesicles due to a very early stage of catarrh. It is the most favourable state in which the tuberculosis can present itself and lends itself most readily to treatment and to perfect recovery. A further development of this condition causes still greater collapse of the lung and can be demonstrated by estimating, best by auscultatory percussion, the height of the apex posteriorly. The affected side can then be shown to be distinctly lower than the healthy side. Such a condition is naturally of somewhat less favourable prognosis, but frequently is recovered from. But the future of the case is much more doubtful if adventitious sounds in the form of râles are found, and not infrequently they can only be detected after cough. I think myself that the finer the râle the more favourable should be the prognosis, coarse and almost bubbling râles indicating a more intense and more advanced catarrh. Obviously, also, the greater the lack of percussion resonance the more unfavourable should be the opinion, but with one reservation—namely, in the condition of so-called "emphysematous phthisis," which will be mentioned below. The above include most of the signs met with in this stage.

But their localisation is of extreme importance. Most frequently the signs are present at the apex of the lung. We hear at times of basic tuberculosis, but this is very rarely of primary origin. Out of 22,000 persons (of whom roughly speaking 19,000 were cases of pulmonary tuberculosis) who passed under my hands in the out-patient room of the Brompton Hospital, I found only some 60 cases which I could believe to have originated as a primary tuberculosis of the base of the lung. This rarity is unfortunate, for such an onset of the tuberculosis in my experience bears a fairly favourable prognosis, not only as to the probability of cure, but also as to slowness of course and the liability of infection of other

portions of the lung. I speak here of primary tuberculosis of the base and not of tuberculosis grafted upon a previous unresolved pneumonia which will be considered later.

What I have said as to the rarity of basic tuberculosis may appear somewhat startling and other observers have rated its frequence more highly. But I draw my conclusion entirely from my own experience of the 22,000 cases mentioned. Since, as I say, this form of tuberculosis bears a favourable prognosis it is not out of place to consider how we can be certain of its presence. Without the greatest care we may assume that a lesion of the base is primary when it is really secondary to one of the apex. The lesion of the apex, although primary, may be very slightly marked—so slightly as to escape the examination of the most competent observer, while the basic and secondary lesion may be very active and well marked. But a secondary lesion of the base, as I will show hereafter when discussing the spread of tuberculous lesions, bears a very unfavourable prognosis, as indicating an advanced condition of the process. Now the position of a basic lesion at the upper part of the lower lobe or near the large branches of the bronchi should at once raise the suspicion that it is of secondary nature and should lead to a still more careful examination of the apices, for it is in this position that, by at least two of the methods of spread which I shall have to mention, such lesions occur. On the other hand, the more favourable primary basic lesion is generally situated in the lower parts of the lower lobe.

So far I have dealt with the position of a primary lesion in the upper and lower lobes respectively. But in the right lung we have a third lobe, the middle lobe, and occasionally it happens that this third lobe is in the left and not in the right lung. I need not here describe at length how one can define the limits of these lobes. Certain landmarks have at times been given for them, but they are very uncertain, and I have formerly demonstrated to another society and published elsewhere how the limits of the lobes can be located with the greatest accuracy by the method of auscultatory percussion. Roughly speaking, the middle lobe lies below the right nipple, but if a primary lesion be located below the left nipple I think it very desirable at once to determine by the method mentioned whether there is in that instance a middle lobe of the left lung; and here is my reason for mentioning this matter in connexion with prognosis. My colleague, Dr. Mitchell Bruce, once stated in a clinical lecture that he found that tuberculosis "beginning near the breast" was generally rapidly fatal, and with this I almost entirely agree. But I would further define the locality and say "beginning in the middle lobe," which, of course, would be most frequently on the right side. Tuberculosis may begin "near the breast" on the left side and yet not be in a misplaced middle lobe, but in the lower part of the upper lobe, and I have found, but of course

only in a small number of cases, that the prognosis of such a lesion does not differ from that beginning in any other part of the upper lobe. But given that the primary lesion under discussion is really in a middle lobe, on whatever side it may be, then the prognosis is distinctly bad. Not that I would go so far as Dr. Mitchell Bruce and say that the tuberculosis is then generally rapidly fatal. Often it is, but when not rapidly fatal it is exceedingly resistant to treatment. This behaviour of the middle lobe is also marked in the case of secondary lesions, as I shall again mention in dealing with the spread of lesions in the second and third stages, and why it should be I cannot say. I surmise, however, seeing how obstinate also is œdema occurring in the same part, that it may be due to some anatomical or physiological difference in the blood-supply of this small lobe.

So far, we have discussed the prognosis of a simple and single tuberculous lesion in its first stage, and we must now consider the prognosis when there is more than one initial lesion, and we may at once decide generally that the more numerous the initial lesions the more unfavourable must be the prognosis, and still further, that the more widely distributed such lesions the worse the prognosis, while multiple lesions limited to one lung will warrant a somewhat more favourable opinion than when both lungs are affected. But here again, as I have mentioned above, we must be careful not to confuse secondary with primary lesions, for bad as the presence of secondary lesions may be, it is not so bad as that of multiple primary lesions. I have already hinted at how localisation will help in this decision and that this will be more fully discussed in dealing with the later stages of the process. But I may here point out that a lesion of the extreme apex of the lung must be almost necessarily primary. Often both apices are affected at the same period or within a very short time of each other. But even when disease has progressed extensively and for some time in one lung, the apex of the other lung may be attacked by an initial lesion. It is true, as I will show in dealing with methods of spread, that it is just possible for a lesion of the apex to be produced by infection from some other part through the blood-vessels, though this is improbable, and even if it should occur, the effect is almost identical with that of the onset of an initial lesion.

The bad prognosis of multiple initial lesions has as its basis, not only the greater damage done to the lung tissue and the probability of still further damage in the future, but also, and this is probably of greater importance, the intensity of the tuberculous poison and the great vulnerability of the system which such multiple lesions indicate. The height of such intoxication and vulnerability is reached in two forms of onset of pulmonary tuberculosis which I will now mention. The first I do not remember to have ever seen described before, though I have met with it frequently, and

I would venture to call it the multiple pleuritic onset. The patient after a short period of ill-health, accompanied usually by fever of some kind, comes under the notice of the doctor because his friends think that there is something wrong. Yet the patient cannot be persuaded of this. Nor does he complain of anything more than a vague languor and flying aches and pains which might be, and indeed often are, ascribed to rheumatism or neuralgia. Such patients have generally come before me because their condition was "queer" and no diagnosis of a positive kind could be arrived at. The state naturally requires a most careful examination of the patient and on making this one may find here and there in the chest a slight pleuritic rub. There seem to be no consolidation and no respiratory distress, but the symptoms are most significant of a powerful tuberculous attack with weak resistance, and, moreover, they indicate that the attack is widely spread. I know of no beginning which bears a more unfavourable prognosis. As a rule, in a short time patches of consolidation appear in the neighbourhood of the pleuritic areas, those patches soften and form small cavities, but still more important is the fact that intense, so-called "hectic," fever develops and the whole system collapses, giving way to other developments of the tuberculous process with a rapidly fatal ending.

The second most serious form of beginning is that which in its ordinary development has been described by Dr. Mitchell Bruce as "emphysematous phthisis." It is true that Jaccoud of Paris and also before him Stokes of Dublin described what I think was the same condition as the "suffocative form" of acute tuberculosis. At least, from the descriptions they give I think that this is so. But they did not recognise it as essentially a lung condition nor did they appear to find that it might pursue a somewhat more chronic course than that of, say, acute tuberculous meningitis or acute tuberculous peritonitis, with which they classed it. But Dr. Mitchell Bruce has described accurately the whole disease. It is acute in its onset and course. The patient complains simply of cough, choking in character, great difficulty of breathing, and on physical examination nothing can be found but the ordinary signs of emphysema. The sputum is bronchitic, mucous or muco-purulent, yet if the physician be on his guard and further examines it, he will find the tubercle bacillus. The temperature may be normal, yet sometimes, fortunately for the physician, it is raised irregularly and this should cause a suspicion of the nature of the case. Further, and these are most important points, the patient wastes and becomes progressively weaker, his appetite fails, and none of the ordinary remedies for bronchitis and emphysema seem to have any good effect. So does the case go on for a short time until at last there come an outbreak of physical signs, patches of pneumonia,

and afterwards of mal-resolution of tbe same, increased fever and weakness, and finally break-down of botb lungs with its nsual accompaniments and deatb. This is one of tbe most serious of beginnings for tuberculosis of the lungs.

And yet I mnst mention anotber wbich resembles each of the above in type and to whicb I hesitate to give any special name. Let me describe first wbat I think is not only its particular patbology but also that of all tbe preceding forms, since such a consideration will help us to a proper understanding and will, I think, fitly conclude tbis part of our subject. The amonnt of physical signs in any individual case indicates, not the intensity of the tuberculous poison by which the system is invaded, bnt rather tbe reaction of the tissues to such an invasion—tbe "chemiotaxis," as it is called by modern pathologists. Tbe symptoms, on the otber hand, are produced by the products of the invasion—to a certain extent, it is true, by tbe over-action of tbe body involved in the chemiotaxis—but to a greater extent by the poisonons action of tbe tubercle bacillus and its belping germs. By rnle of thnmb I have arrived at this conclusion which I put to you as being a useful gnide: "If the symptoms are out of all proportion greater tban the pbysical signs, think badly of tbe future of the patient." You will see tbe rationale of tbis. It means, looking at the matter as I bave stated it above, tbat in such a case the action of tbe bacillus and its accompanying poison is in advance of tbe resisting power of the lung tissue. I admit that this idea of the patbology is not unopen to criticism and is, indeed, faulty. But I give it as a probable explanation of the facts wbich I will now describe. Not seldom one meets with cases in whicb for even a considerable period symptoms are very marked and so severe indeed as to keep the patient confined to bed for months. The temperature is raised regularly and irregularly and often, too, intermittently. Emaciation is continuous, appetite disappears, and weakness is extreme. Tbere may be no cough, or such as may be present is so inconsiderable as to be almost overlooked, and so the case goes on, while no matter how carefully the physician examines he cannot find more tban the most unimportant physical signs. Possibly tbere may be a little œdematous crackling at the borders of tbe lungs, an occasional broncbitic sibilns, even a few streaks of blood, which may be attribnted to a congested throat—and these are all. Often I have known such a condition attributed to persistent influenza, not infrequently to subacute rheumatism, and sometimes to sheer nenrotism. Yet I offer you a warning to beware of giving a favourable opinion of such cases. Time after time I have seen this apparent quiescence of lung disease give place to a furious outbreak of lung destruction and an early death. If I were to give a name to tbis type I would call it "latent pnlmonary tubercnlosis." The tuberculosis itself is active enough, but its pulmonary

characteristic is latent and therefore differs from that of the pleuritic and emphysematous forms already mentioned.

Hitherto we have dealt with the indications for prognosis to be drawn from the character of the physical signs and the method of their presentation in the invasion stage of the disease. Let us now turn to a consideration of the conditions which precede the outbreak and which may possibly conduce to its occurrence. I cannot deal with all these, but I will discuss with you the more remarkable points which appear from an examination of the 22,000 cases which came under my charge in the out-patient room at Brompton.

Simple chlorosis is rarely an antecedent to tuberculosis, and, indeed, in general effects the two conditions are very different. Chlorosis is commonly accompanied by an accumulation of fat, tuberculosis by its diminution. This has been observed many times before now and must be well known to all of us. But I have carefully noticed the progress of an initial tuberculous lesion in pale and in florid patients respectively. Most of our patients are pale, but not infrequently one finds tuberculosis presenting itself in the most florid and apparently full-blooded subjects. In judging of this I try to make no mistake between the apparently full-blooded and those who, really anæmic, present the flushed cheeks and delicate complexion so often and rightly considered to be indicative of a tuberculous tendency. *Cæteris paribus*, I find that the florid subjects seem to behave worse in their resistance to the tuberculous invasion than do the anæmic subjects. They are certainly more prone to suffer from severe hæmoptysis, from recurrent destructive pneumonias, and from high fever. Again, they are the more likely to present latency of the physical signs, which, as I have above pointed out, is of grave significance. On the other hand, the anæmic subjects much more commonly have shown a slow progress of the disease. Yet in estimating the prognosis one must think, too, of the effects of treatment in such cases, and certainly one finds that the florid patients, when once got hold of, are more amenable to the ordinary methods of treatment than are the anæmic ones. To summarise the above remarks I would say that, viewing the much larger number of anæmic than of florid patients who are attacked by pulmonary tuberculosis, the percentage of cures and of slow progress of this disease is very much greater in the anæmic than in the florid. Given that a florid person is really attacked by pulmonary tuberculosis and that this is decided by perfect observation, the prognosis of his case is on the whole more serious than is that of an anæmic person similarly attacked. An explanation of this may be found in a remark of Sir William Broadbent in his book on "The Pulse," that such florid patients are generally the subjects of vaso-motor atony.

Deformity of the chest undoubtedly predisposes to tuberculosis of the lungs, and this, too, whether the deformity be

due to simple scoliosis or to kypbosis from pre-existent tuberculosis of the vertebræ. From whatever cause the deformity results, it greatly increases the gravity of the prognosis when once tuberculosis of the lungs has established itself. This bas an obvious explanation. The deformity interferes with respiratory movement and bence witb tbe circulation of blood through the lungs. The tubercle bacillus has then a better chance of attacking the lung tissue without tbe protection of the tissue by a free flow of nutrient blood. The result is almost invariably, as I have found, a rapid destruction of lung tissue and also an even more rapid decrease of the body powers consequent upon the general feeble vitality. The prognosis is bad.

Such deformity of tbe cbest is often, as I have mentioned, due to an actual tuberculous disease of the vertebræ, and tbis leads one naturally to tbe consideration of other pre-existent tuberculous affections, and especially to the prognosis of tuberculosis of the lungs following and accompanied by tuberculosis of the lympbatic glands. Before the nature of the patbological process in such glands was accurately known the condition was described as the scrofulous diathesis, and undoubtedly tbe patients who suffer from it constitute a group differing greatly in many points from those wbose lungs are affected at tbe beginning of their disorder. What is the essential difference between these two rough groups I do not know, but that tbere is such difference I am well aware of. The danger to a patient of possessing such tuberculous glands is certain. Nevertheless, judging from my own experience, I must say tbat tbe progress of a pulmonary tuberculosis secondary to a pre-existent glandular affection is much slower and consequently more favourable than wben the lung tissue is primarily invaded. The glands, we know, form a resting-place for the tuberculous poison, a resting-place fairly well cut off from the rest of tbe body by bardened inflamed tissue, and, still more important for the purpose of prognosis, a resting-place wbich can often be easily removed togetber witb its contained poison. The surgeons now deal freely witb such glands, and absolute ablation is the best remedy for them. The possibility of tbis greatly increases the probability of cure of any lung affection wbich may accompany tbem. They can also be removed by other means, but, to trench upon the subject of my later lectures, let me at once say that nothing can be worse for the future of the patient than the so-called dispersal of such glands by painting witb iodine or rubbing witb iodide liniments. The glands then may disappear, it is true, but very frequently only to spread their contained poison elsewhere in the body and to increase any lung trouble wbich may exist. I sball eventually have to mention bow such glands can safely be dispersed, and in a marvellous manner, by the administration of nuclein by the month, and tben without such bad effects as I bave mentioned. But the presence of such glands seems to me to be, on the wbole,

a favourable element in the prognosis of a tuberculous lung affection in that they can be usually easily removed, that their removal takes away an important focus of tuberculous poison and leaves the lung tissue unhampered in its efforts to fight the bacillus, and, lastly, that the diathesis, if we must call it so, which is displayed by such lymphatic tuberculosis, is generally combined with a similarly slow process of tuberculosis in the lungs.

Time will not allow me to do more than merely hint at the influence of the presence of lymphadenomatous glands and also of lymphadenomatous and malignant disease of other structures upon the progress of a tuberculous disease of the lungs. Suffice it to say that the combination is uncommon and the gravity of the more or less malignant disease entirely overshadows that of the tuberculosis. The connexion of the two series of disorders, uncommon as it is, is extremely interesting, and the out-patient department and also the post-mortem room at Brompton Hospital have given me matter which might well be discussed, but almost entirely from the pathological and not from the clinical standpoint. Again, too, I will not deal here with the co-occurrence of cardiac disease and tuberculosis of the lungs, or their mutual affection of the prognosis, for this has been treated very fully by others.

But amongst the most important disorders (from the prognostic point of view) which may precede an outbreak of tuberculosis of the lungs are pleurisy, serous or purulent, and pneumonia. I have already mentioned how serious is the outlook when pulmonary tuberculosis first shows itself by the presence of scattered patches of pleurisy. I do not wish to refer here to this particular form of outbreak, but to those cases in which a pleurisy, generally with effusion, precedes the onset of the tuberculosis. It is, nevertheless, remarkable how often, judging from the results of many observers, an apparently simple pleurisy with effusion is really tuberculous in nature, as evidenced by the finding of tubercle bacilli in the exuded fluid. Yet we know very well how comparatively seldom such a pleurisy with effusion is followed by more general pulmonary tuberculosis, and I would especially call your attention to this fact as giving ground for the belief that simple pleurisy with effusion need not necessarily bear with it a bad prognosis for a tuberculous subject. Undoubtedly, a pleural effusion, not previously ascertained to be tuberculous, is in some instances followed by an outbreak of tuberculosis in the apex of the lung of the same side, and probably this is due to malnutrition of the lung consequent upon its disordered circulation. But from actual observation I can say that such outbreaks of tuberculosis are rarely so serious in their actual attack or in their further progress as those which have not been preceded by such an effusion. Again, departing somewhat from our order of discussion, I will mention here that the occurrence of pleural effusion in the

conrse of a pulmonary tuhercnlosis, and especially in the stage of invasion, seems to he actnally of henefit if only that effusion he not removed. It is well known at the Brompton Hospital that a simple plenral effusion in a tuhercnlous patient is hest left alone if it does not seem to be unduly hampering the respiratory apparatns, and a prohable explanation of this fact I will give under the head of Treatment.

When the pleuritic finid is not serons but purulent, when, in fact, an empyema has occnrred and has heen removed hy operation, it is again remarkahle how seldom this is followed hy pulmonary tuberculosis if we take account of the large number of cases of empyema which come under treatment and are permanently cured. Yet when tnberculosis does hreak out after empyema its course is usnally rapidly fatal, a result which one might expect from the fact that the original empyema is itself the result of a very low vitality, and this will of conrse have its dne influence upon a following tnherculosis.

Pneumonia is an essential element of pulmonary tnhercnlous ontbreaks, and, indeed, gives rise to nearly all the physical signs from which we form our diagnosis. But we at this point must deal with pnenmonia as a precedent of the outbreak—a pneumonia not of itself tuherculons, bnt occurring in a person predisposed to tuhercnlosis. I am not much afraid of a tuberculosis of the lung which follows upon an ordinary croupous pnenmonia. But I must be careful here to make myself perfectly understood. I am speaking of the prognosis of the tuberculosis and not of that of the pneumonia. Naturally, tuberculosis is a danger to a person who is snffering from croupous pneumonia and its possible outbreak greatly increases the gravity of the prognosis of the pnenmonia. But I think the previous existence of a simple croupous pneumonia does not materially affect the prognosis of a consequent tnbercnlosis. Most cronpous pneumonias affect the hase of the lung and tnberculosis consequent to them is, as I have already stated, not only rare, but slow in progress. Pneumonia affecting the apex of the lung, beginning in the ordinary turbulent way of the croupous affection and not initially tubercnlous, if it does not canse immediate death, is generally followed hy complete resolution of the lung, and, indeed, more freqnently and completely than the same affection of the hase. The pneumonias of the base which are followed hy tuberculosis of the same part are much more frequently found in children, and for this reason, too, the prognosis is the more favonrable.

I wonld say a few words abont tnberculosis of the urinary organs followed hy tuherculosis of the lungs. It is curions that urinary tuhercnlosis, beginning as snch, shonld remain for so long a time—and this is a fact in its history—located to the urinary organs alone. This seems to be the case, no matter where snch urinary tuberculosis first shows itself, whether in the kidney, the ureter, the bladder,

the urethra, or the vesiculæ seminales. Probably, it seems to me, the reason can be found in the fact that the urinary organs are mostly developed from a different embryonic layer than are the lungs and most other of the internal organs. Yet towards the end of such cases one does meet with pulmonary tuberculosis. Invariably, I have found that the lung trouble plays only a very minor part in causing the end of the patient—the pulmonary tuberculosis, as such, bears a favourable prognosis. Unfortunately, this is of not much benefit to the patient, for by the time the lung trouble has developed his condition is otherwise hopeless

My out-patient records afford some evidence too of the effect on prognosis of previous tuberculous disease of the lungs in the same family, though let me say that I inquired only into the history of father, mother, brothers, and sisters. Incidentally they indicate how rarely such tuberculous family history could be obtained if we take into account the large number of tuberculous cases included in the records. This supports the view held by modern hygienists that heredity does not play so important a rôle in the causation of tuberculosis as does actual infection. Yet the influence of such hereditary tendency can by no means be ignored, for I find that whenever present it very seriously affected the gravity of the case.

Another point, too, which crops up in the examination of this long series of cases is that but few of the patients affected by tuberculosis led open-air lives, and although I cannot actually bring statistics forward to prove this point, yet it was my impression that those exposed to inclemencies of weather, such as navvies, bricklayers, and so on, did far better than did those who had the opportunity for keeping indoors. I lay, however, but little stress upon this observation, for obviously such as had those occupations were the more robust of the patients. And in contradiction to the apparent conclusion let me say that a certain number of my patients were Polish Jew tailors from the East-end, nearly all of them in a terrible condition of poverty and dirt, and living, as we know, amidst the most frightful unhygienic surroundings. Only few of these had tuberculous affections, but they suffered greatly from bronchitic and other catarrhs.

LECTURE II.

Delivered on Nov. 8th, 1900.

MR. PRESIDENT AND GENTLEMEN,—In my last lecture I discnssed with you how tbe prognosis of tuberculosis of the lungs in the first stage of its course, that of "invasion," may be judged from the physical signs and the localisation of the lesions, and I considered, also, what effect pre-existent affections might have upon the future of the patient. Let ns now pass on to the indications which may be given to us by individnal symptoms and complications, still confining our discnssion to the "first stage." The symptoms accompanying this stage are many and all are at times important for diagnosis, bnt those which help us in prognosis are but few and they may be classified under the heads of Pyrexia, General Weakness, Digestive Disturbances, and Hæmoptysis. I have mentioned how the conditions previously considered require care in their estimation before one can found a prognosis upon them. But still more is this necessary in the case of symptoms. Not one of them alone is of much valne, but I must point out to you how, when combined togetber or with the other conditions, they may be of some assistance. Pyrexia may be entirely absent, even thougb the temperature in a doubtful case be taken every four hours. So much, one might say, the better for the patient. So much the better, too, might we think the matter if there were but few physical signs, and those, too, limited to one particular area. But caution must be observed here. Such a state of things may be merely the result of a lack of reactionary power on the part of the general system, a lack of protective power; and if together with the conditions named tbere be tubercle bacilli in the sputum and extreme general weakness we can only consider the condition as very grave and indicating an unresisted attack of the bacillus. In no short time one frequently meets with a furions outbreak and rapid destruction of lung tissue.

But given bacilli in the sputum and little or no pyrexia, the local manifestation limited, but with the general strength well maintained, the prognosis is good. The indications are that the attack is not powerful, the resistance to it is good and not fully called forth. For we should, let me remind you, consider the fever as the result either of bacillary poison or, on the other hand, of inflammatory

chemiotaxic reaction. It is impossible to entirely differentiate the two, but I would provisionally put it to you that the maintenance of body strength, together with the presence of localised physical signs and the lack of marked pyrexia, would indicate a healthy reaction, while, on the other hand, localised and even very limited physical signs, with lack of marked pyrexia but with great diminution of physical strength, would show a lack of resistance to the bacillus, not only on the part of the lung, but on that of the whole general system.

Yet, leaving the question of maintenance of general strength out of the discussion, one may roughly say that the higher the pyrexia the worse the prognosis in this stage, and *vice versâ*. And yet once more we must use caution, especially with neurotic patients. Such patients may show a very high temperature when there is really nothing much wrong with them, and in the absence of physical signs their condition is very confusing. Nothing but great experience can prevent the physician from being led into error in diagnosis by such a physical state, and the same error is easily made in prognosis. It happens not infrequently that tuberculosis of the lungs, like enteric fever, may have a most turbulent outbreak and very soon lapse into a very ordinary mild and tractable attack. Now, my colleague, Dr. Kingston Fowler, has shown that the only form of pyrexia which can be absolutely said to be tuberculous is that in which the morning temperature is higher than that of the evening. For the diagnosis of pulmonary and other forms of tuberculosis there cannot be any question of the value of this observation, and especially when other indications are doubtful. For prognosis, too, this sign may be of use as indicating a very pronounced tuberculous poisoning. On this point even the large record of out-patient cases which I have used cannot help us, and we must appeal for facts to the in-patient department. Since taking the charge of in-patients I have paid special attention to the matter, and at present for convenience of observation the evening temperature is marked on the charts in red and the morning temperature in black. It is very remarkable, however, how very rarely in the course of a case of pure tuberculosis this sign appears. Nor is this to be wondered at when we remember the many known causes of the pyrexia. Tuberculous infection and its accompanying tissue-reaction or chemiotaxis are, in the first stage, causes of fever. Whereas later we have added to them poisoning by the staphylococcus and pneumococcus. Pyrexia due to tuberculous poison alone must necessarily be rare and not always is it of the reversed type. Therefore, it must be only seldom that the pyrexial condition can help us in prognosis. But somewhat approaching this type is a pyrexia in which the morning temperature never reaches the normal, albeit the evening temperature may be only

slightly higher. Snch a pyrexia, even alone as a sign, is of very unfavourable augury, and the higher the morning temperature and the nearer it approaches to the evening temperature the worse is the outlook for the patient.

In regard to the foregoing remarks it is necessary that I should say that they refer to temperatures taken in the mouth. For really scientific results one should place the thermometer in the rectum and this is done now, I believe, in most of the open-air sanatoria. But in ordinary practice there are obvious objections to this method and I have striven here to give opinions which may be made use of only in ordinary practice.

General weakness at the commencement of a tuberculous attack mnst manifestly be harmful, and indeed, as I have hinted above, increases greatly the gravity of other symptoms. Particnlarly (if one may analyse the state) must weakness of cardiac and vaso-motor action be considered a bad sign. The patients who have blue and cold extremities almost invariably do badly. Nor does this remark contradict what I have previonsly said as to the occasionally bad prognosis to be given to florid snbjects, for often that florid appearance is a sign of vaso-motor weakness and not of a healthy circulation. This feebleness of circulation, and with it of the general system, carries with it a bad prognosis, not only because it indicates a prospective lack of resistance of the tissnes to the tuberculous poison, but also because it usually interferes greatly with such valuable means of cure as over-feeding and residence in high altitudes and the open-air, valuable as at times these remedies may be in counteracting this very condition. The same must be said of digestive disturbances accompanying an attack. They interfere with the application of systematic treatment. But I should like also to say a few words abont the prognosis of cases which show gastric derangement as their first symptom. It has long been known that an irritation of the pneumogastric nerve-endings in the lungs may first show itself by a reflex irritation of the endings of the same nerve in the stomach. The diagnosis of such an occurrence is often very difficult, since even for some little time the lung lesion may be so slight as to be indiscoverable on the most careful examination. But sooner or later the lung lesion does show itself, and in my experience snch cases eventually do badly.

Let us now turn, however, to one of the best known of the symptoms which accompany the earlier stages of pnlmonary tuberculosis—namely, hæmoptysis. This symptom is only too well known and causes far too much alarm. Yet it occurs so often in other disorders that I think one may say that hæmoptysis alone is most frequently not caused by lnng disease. But given that it actnally is produced by lung disease in the earlier stages, at least its presence does not necessarily increase the gravity of the prognosis, even though the output of blood be somewhat

copious. Repeated small hæmoptyses are often a relief to an over-congested pnlmonary area. But I would not say the same of repeated copions hæmoptyses ; such give us evidence of severe aud long-continned lnng trouhle and increase the gravity of the case. Oue single large hæmoptysis, without pyrexia and without signs of any extensive lung lesion, is of comparatively little importance, hnt even one large hæmoptysis together with pyrexia should canse misgiving in the physician's mind as to the future of his patient. I speak here, of conrse, of hæmoptysis in only the initial stage. In the later stages this complication is of mnch more importance. Let me also call your attention to a mode of occurreuce of hæmoptysis which is often quite nnnecessarily alarming. It has received very little attention. The method of treatment of early tuberculosis has invariably heen one of high-feeding in some shape or form. Now, this necessity for the high feeding in time disappears as the tuherculosis disappears, and yet such patients persist in such feeding even to middle life and old age. Then hæmoptysis occurs as it would do in a non-tnberculons patient who might have been snbjected to the treatment and is really a safeguard to the geueral vascular system. Such hæmoptyses are never accompanied by pyrexia.

So far I have dealt only with the first, or "invasion," stage of tuberculosis of the lnngs, and now we come to the second stage, or that of "progress." Let me, for fear you forget, remind yon of the method which we are attempting to pursue. First the attack and its called-for resistance from the tissnes, and now the giving way of the tissues before the attack. The signs of snch giving way need not delay ns long, for they are of but little help in prognosis, however important they may be in diagnosis. They have hitherto been called signs of "softening," meaning by that (if only we took a rational view of the process going on in the lungs) a giving way of the inflammatory or chemiotaxic reaction of the tissues to the invasion of the germ. Our prognosis must depeud upon the estimation of how far it is probahle that the invasion will go, how far the tissues can resist it, and what the effect of the hattle may he, what damage will he done to the grouud and the system in general hy the invader and by the reqnisite reaction of the invaded. I think we must now inquire how far the invader has damaged the tissue, aud how much farther he is likely to go in the future, and all this hinges upon whether the general system, aud with it or through it the iuvolved tissue is likely to give way before the iuvadiug germs. Let us look at the matter first of all in the view of ueighbouring extension. This is a question of physical signs, and now we must iguore many which I have mentioned as occurring iu the first stage. Pleurisy is here of little importance ; small râles or crepitations do certainly show extension of mischief, but what we onght to be most on the look-out for are the bubbling large râles with which

we are all well acquainted. I must not here enter into their pathology at any length, but I may say that a better name for them is "echoing" râles. They echo or resound, and I cannot myself distinguish the essential mechanisms involved in the two terms, either generally or in their non-specific application. I have thought over what Helmholtz and other authorities have written on this subject and have studied how their views might affect the physical signs in question. But I cannot see that there is any difference between "echo" and "resonance," for, at any rate, our purpose; and coming to the immediate point, which is first one of diagnosis and afterwards of prognosis, I think that these râles, bubbling, resonant, echoing, metallic or consonant, as they have variously been called, are under all these names indicative of a condition of tissue in which there is softening of inflammatory products in a cavity of some certain size. This, I conceive, is the pathology of such a condition. In my experience as pathologist at the Brompton Hospital I have repeatedly found such a condition post mortem after having suspected its presence during life. The cavities are not large, they could not be diagnosed as such during life, but they were there in the site of the "echoing" râles. Sometimes they are diagnosed, really only on suspicion, as "diffused cavitation," but no one could be sure of them during life as cavities. Nevertheless, I think this form of râle is produced by the echo or resonance of a crepitation in a small cavity of the tissue, and thereon depends its value in prognosis. The echoing râle means the giving way of the tissue and the prospective continuance of such action makes its prognostic value. Given, then, the existence of a lesion of the lung with all or some of the signs which we have mentioned as accompanying the first stage, the presence of the râles under discussion indicates progress of the germ and the extension of its action beyond the parts originally affected, a further invasion of, at least, the lung tissue, leaving out of the discussion the affection of the general system which the tubercle bacillus may hereafter invade. I have herein made an excursion into pathology but I have already told you that pathology should give us our basis for prognosis and also for treatment. A case comes before us, diagnosed by ourselves or by others as tuberculosis of the lungs in a somewhat advanced stage, meaning, thereby, that the first stage has passed! The point of our prognosis must depend upon how far can the passage of the germ proceed, without further deterioration of the lung tissue. This as regards the second stage and no more!

Here I come to the matter hinted at in my former lecture, the method of progress of tuberculous lesions in the lung. I have mentioned hitherto that I would refer to this as a matter of importance and once more I appeal to facts as offered to you in the cases which I show from my records at the Brompton Hospital. We have to consider the question of how an invasion once

established in the lungs can be carried to other parts of the lungs and to other parts of the body, for in the matter of this extension rests our prognosis of the case, in the stage under discussion. It may seem at first sight only a question of pathology, but on it hinges our full diagnosis and therefore prognosis. Extension of a tuberculous lesion of the lungs may take place by means of (1) simple contiguity of tissue ; (2) lymphatic absorption ; (3) bronchial insufflation—a matter of the greatest importance ; (4) venous conduction ; and (5) arterial conduction ; and while our first concern must be the condition of the lung, we must also consider how far our prognosis may be affected by extension to other parts, for it is in this stage that this extension is most important. We will take the methods in the order in which I have mentioned them.

1. *Contiguity of tissue.*—We can estimate this by the localisation of those râles which I have already discussed and not necessarily by the extension of consolidation which may or may not accompany them. The more widely spread are those râles from the point of primary infection the more extended is the tuberculous infection and therefore the more serious is the prognosis for the patient, since such an extension means that the resistance is giving way before the invasion. But it is most remarkable how the resistance is assisted by the anatomy of the lung. For a very long time the lesion, extending only by mere contiguity, remains located to one lobe of the lung. I mentioned in my last lecture, as I shall have to mention often in this, how important it is to localise the lesion in regard to the lobes of the lung and I have described how this can be done accurately. Given, then, that the lesion has extended from its original site, the prognosis is good (or at least as good as it can be) if the lesion does not pass beyond the lobe in which it took its origin. Of course, I am speaking here of the lesion itself and not of the symptoms which may accompany its progress. These may be of extreme importance and will be mentioned later. But sooner or later the limit of the lobe is passed and this is by means of the second method of extension.

2. *Lymphatic absorption.*—Undoubtedly this plays a great part in the first method. No one can doubt it who has carefully examined a section of the lung under the microscope in the later stages of croupous pneumonia. There one can see the lymphatics which surround the bronchi, and which ordinarily are almost empty spaces, to be distended with the granular débris absorbed from the alveoli. In tuberculous pneumonia that débris contains the tuberculous poison and by means of it, the poison is spread to surrounding parts and with it the infective agent and its accompanying lung-damage. The inflammation leads to adhesion between the lobes of the lung ; those adhesions include lymphatics and thus at last we have the natural barrier of the lobes broken down. We

cannot hope to detect the exact moment of this occurrence hut we can detect very soon any important development of mischief. When we do so we know that another lohe of the lung has heen invaded and that there is no further harrier on that side, to the progress of the disease. Given, then, that the lesion has extended from one lobe to another hy direct contiguity or by lymphatic absorption (and prohahly hoth methods are concerned in the process) the prognosis is had. But mere extension of the initial lesion, had as it is, is not the worst which may happen to the patient hy this extension. I have myself on a few occasions traced out similar tuherculous lesions to the hronchial glands and further. On one occasion I traced a tuherculous lesion of the ahdomen hy way of the receptaculum chyli through the thoracic duct and therehy to the venous circulation. The case was published some years ago under the title of Chylous Ascites by Professor Whitla of Belfast. There can be no douht that by means of the lymphatics the tuherculous poison is spread to remote parts of the hody and the possibility of such spread increases the gravity of the prognosis in this stage of tuherculous affection of the lungs. The detection of the results of such spread is beyond our present suhject, hut its occurrence marks a very late stage of the disease. The general spread of the tuherculosis occurs also in other ways and must he discussed apart, though its prognosis, when once it has occurred at all, is usually fatal and will not detain us more than a few moments when it has to he further mentioned.

3. *Bronchial insufflation.*—The third method of extension, hy hronchial insufflation, is, as regards the lungs themselves, of hy far the greatest importance. Many years ago Carswell of University College described the grape-like masses of pulmonary consolidation and caseation which occur in tuberculosis of the lungs. They are figured in his own plates and also in the Atlas of Pulmonary Diseases puhlished hy the late Dr. Wilson Fox. Wilson Fox's Atlas and also his hook were unfortunately delayed in puhlication, hut like Dr. Walshe's Diseases of the Lungs they are invaluahle records of accurate ohservations which now, even with our later ideas of pathology, cannot be neglected hy any searcher after facts. Carswell and also Wilson Fox did not see the significance of "Carswell's grapes," as they have been termed; but a study in the post-mortem room and a reading of Dr. Ewart's Anatomy of the Bronchi will, I think, explain their occurrence and indicate how they will help us in prognosis. These "grapes" occur usually in the lower lohe of the lung and in the middle part of that lohe. In the post-mortem room we see them in the centre of the lung and also frequently reaching to the surface. It is only when they have extended to the latter-mentioned position that they can be detected during life. Without

doubt they are due to infection of the lower lobe of the lnng by excretion insufflated through a bronchus, excretion which ought to be ejected, but is not, and which in the inspiratory effort which follows cough is drawn into the neighbouring bronchi and thence infects other portions of the lung. Such infection certainly may occur in the upper lobes and the pathological appearances warrant this supposition, but we cannot determine this clinically. Yet we *can* determine the presence of such a lesion in the lower lobes during life and it is of the greatest importance for our prognosis. A patient who has snffered, as we have previonsly determined, from tuberculosis of the npper lobe on one or other side, is found to have a lesion in the lower lobe of that or the opposite side and with the incidence of this lesion there is an increase of the pyrexia and of the general symptoms. The lesion in question will be found—care as to localisation being observed—not in the upper part of the lower lobe, where it might be due to direct extension as already mentioned, not in the lower part, where it might be a primary basic tnberculosis as described in my first lectnre, but in the mid-way of the lobe and indicated by dulness and râles such as have characterised the primary lesion.

I have not been able to satisfy myself as to upon which side such an infection may be expected from a lesion of either specified apex. One would reason that it should occur on the opposite side in view of its pathogeny, yet I find from my records that its choice of side seems to vary. It was this lesion which I had in my mind when, in my first lectnre, I warned you to be careful in your diagnosis of a primary basic tuberculosis. The initial lesion in the upper lobe may be very slight, almost imperceptible on the most careful examination. and the secondary lesion may appear to be very advanced. Yet the localisation of the latter in the middle part of the lower lobe should point out its character. Such a lesion shows a very important extension of the initial mischief—important as to the actual mischief done, but still more important when we consider that it is a new focus of disease, and extensible by its contiguity (through lymphatic absorption and by the the other modes soon to be mentioned), not only to the whole of the lower lobe of the lung, but to remote parts. The finding of such a lesion undoubtedly greatly increases the gravity of the prognosis. Further, I would remark that it has appeared to me that whatever may be the state of the primary lesion the secondary lesion seems to advance with greater rapidity, possibly becanse the poison has been placed on soil which has previously been weakened by the general disease, and because, too, there are no barriers to the progress of the poison such as in time are formed in the primary lesion by fibrous cicatricial tissue.

The other two methods of extension are not so obvious and yet are of importance in pathology. Not, however,

to so great an extent as to help us much in prognosis, though it is right that we should recognise them. In the course of a case of tuberculosis of the lungs we sometimes meet with strange and apparently unaccountable fresh outbreaks in spots remote from the initial lesion. No doubt some of these, and especially those which occur at the apex of the lungs, are really primary outbreaks, and it may be convenient here to deal with their prognosis at once. They are most serious occurrences and they mean that the disease has started afresh with all the probabilities which accompanied the first onset. But undoubtedly some such lesions are due to—

4. *Venous conduction.*—The anatomy and physiology of the lungs have not been sufficiently studied by physicians. Especially the circulation of blood through the lungs has been overlooked, and in my next lecture I shall have to show you how it can be taken advantage of in treatment. But as regards pathology let us not forget that the circulation through the lungs is twofold. The pulmonary artery carries blood to the lungs in order that the blood may be aërated, and that same blood is carried back to the left side of the heart by the pulmonary veins. But the lungs have to be nourished and this function may be carried on by the bronchial arteries which come from the aorta. The bronchial veins take the blood, which is effete from having nourished the lungs, to the right side of the heart, and the right ventricle drives this blood once more through the lungs. Now when the lung is infected by tuberculosis this effete blood is liable to be loaded with tuberculous poison from the lung and therefore once more the poison is driven through the lungs, through the pulmonary artery, and, further, may be disseminated widely—far away, possibly, from the primary focus of infection. We must argue from all this that however unfavourable may be the prognosis when secondary lesions arise in such situations as to give us reason to know that they are due to (*a*) direct extension, (*b*) lymphatic absorption, or (*c*) bronchial insufflation, yet scattered new patches due to fresh initial outbreaks or to (*d*) venous conduction are of much more serious augury.

5. *Arterial conduction.*—The last method of direct extension from the lungs, that by arterial conduction, does not essentially concern the lungs themselves but mostly the general system. It has been already spoken about in the previous section in so far as the bronchial arteries are concerned. Also we must remember, as already stated, that the blood taken from the lungs by the bronchial veins, infected probably by tuberculous poison and re-distributed to the lungs, may, with all the other blood of the pulmonary artery, pass through the lungs without further infecting them, but with the possibility of infecting other parts of the body.

Thus we get, not only further infection of the lungs, but also tuberculous meningitis, tuberculosis of the kidneys and spleen, and so on. The prognosis of all these is, of course, most unfavourable.

So far I have spoken only of extension directly from the lung itself, but a most serious matter is the extension of tuberculous mischief by the excretion of the lungs after it has left the lungs themselves, and the only two points with which I intend to deal are the affections of the larynx and of the intestines, for their presence very greatly increases the gravity of the prognosis. Let it be at once dismissed from our minds that tuberculosis of the larynx is ever primary—dismissed, that is, in so far as prognosis is concerned. Tuberculous tumours of the larynx undoubtedly do occur, but they are exceedingly rare. But "phthisis of the throat," as it is called, is practically non-existent as a primary lesion. This matter has been already thoroughly threshed out and the reasons for holding such a view are very concisely given by Dr. Hilton Fagge in his "Text-book of Medicine." They may be briefly stated thus; 1. Most cases of laryngeal tuberculosis can be shown during life to be accompanied by signs of lung mischief. 2. Always laryngeal tuberculosis is post-mortem found to be accompanied by lung lesions. 3. Advanced lesion of the larynx may be accompanied by but slight lesion of the lungs and yet the former may be secondary and the latter primary. 4. The non-finding of lung trouble is no proof of its non-existence, for even the best observers may be deceived in this matter.

As an illustration of the latter argument I may mention a case which occurred in the out-patient department of the Brompton Hospital. A man presented himself one day who had unquestionable tuberculous ulceration of the larynx. He had also cough and all the appearances and symptoms of advanced tuberculosis of the lungs. But the most careful examination by myself and several other medical men who were attending the clinique, failed to find any but the most ambiguous physical signs in the chest. This might have been looked upon as a case of primary laryngeal tuberculosis, yet I was sure it could not be. On two other occasions, an interval of a fortnight elapsing between his visits, his chest was further examined and with the same result. But on his fourth attendance signs of cavity were found in almost every portion of the thorax. The cavities could not have formed in a fortnight. Undoubtedly they were present at his first examination but, from blocking by mucus or from some other condition, escaped detection.

Tuberculosis of the larynx is therefore always caused by infection of the larynx through the excretion of the lungs. Similarly, too, the intestines become infected from the swallowing of tuberculous sputum. I do not speak here of primary tuberculosis of the intestines, which is most common in children, but of the intestinal ulceration secondary to lung disease. That this is due to infection

carried from above is shown by its localisation. It is invariably seen, in its early stages, near the ileo-cæcal valve. During my period of office as pathologist to the Brompton Hospital, Dr. Dodgson and Dr. Soltau Fenwick examined carefully the appendix vermiformis in all the post-mortem examinations. They always found it to be affected when other parts of the intestines were ulcerated and in a not inconsiderable number of cases they found the appendix alone to be affected. This points to the conclusion that the ulceration occurs where the swallowed secretions of the lung are allowed the longest contact with the mucous membrane of the bowel. The symptoms, of course, are those with which you are well acquainted—pain, diarrhœa, &c. The occurrence of this condition carries with it the gravest prognosis, and, indeed, nearly always introduces the fatal end.

As regards symptoms, there are only two which in this stage help us greatly in prognosis, and they are pyrexia and hæmoptysis. This, the second stage, is, unlike the first stage, never without pyrexia, and what has been said of the fever of the first stage applies also to that of the second stage, though without the limitations there mentioned; that the higher the fever, and again the more nearly the morning temperature approaches that of the evening, and the worse is the prognosis, may be taken as a general rule. But still worse is the so-called "hectic" fever, where a morning temperature below normal is followed by an evening temperature of even eight degrees higher. This is a most serious condition and all the more so because, in my experience, no drug has the slightest effect upon it.

Hæmoptysis is a much graver symptom in the second stage than in the first, and is here dangerous. This results from the fact that while the hæmoptysis may still be caused by mere congestion, yet it much more frequently is due to ulceration of a blood-vessel from so-called caseous or suppurative arteritis. The dangers of its occurrence are: (1) loss of blood, a very serious matter in an already debilitated subject; (2) shock with cardiac failure; and (3) fright. The last-mentioned danger has not often been mentioned, and yet I have seen it occur. I differentiate it from the second danger, for I have known death occur from what I could conceive must be this and no other cause when only small quantities of blood have been expectorated or found in the lung tissue after death. There are doubtless other symptoms of the second stage, such as general weakness, emaciation, profuse night-sweats, &c., which are of importance in prognosis, but they have already been mentioned in a former part of this lecture, and they can be comparatively easily controlled by treatment, therefore they do not require detailed discussion here.

The third stage of pulmonary tuberculosis I have chosen to call that of "result" and not "cavitation," as has hitherto been done, and for the reason that "cavitation" is

not the only final result of the tuberculous process, though that result always means destruction of lung tissue. Cavitation is nearly always accompanied by a certain amount of fibrous thickening ronnd the walls of the cavity, and, *cæteris paribus*, the greater the amonnt of fihrosis the less dangerous is the presence of the cavity. But we may get fibroid change without any appreciable cavitation, and these two conditions, "cavitation" and "fibrosis," therefore constitute two separate forms of the "result" stage, each with its own particular elements of danger, and therefore to be distinguished in prognosis.

Pursuing again our former order of discussion we will deal first with the nature of the physical signs. The percussion note obtained over a cavity is the resultant of two conditions, the cavitation and the thickening of its walls, the one causing increased resonance, the other dulness, and hence we get the high-pitched resonance of the cavernous percussion note. Given, then, that we have diagnosed the presence of a cavity by other methods (and I bave elsewhere described how this should be done), then the higher pitched the resonance, and the greater the resistance to the finger, the more favourable is the condition. This view is based upon the idea that such a condition of signs indicates a greater amount of fibrous tissue round the cavity, whicb I have above stated to be a desirable state. Moreover, the presence of "echoing" râles would indicate a complication of the third by the second stage and a further progression of tuberculous action. This, of course, is an nnfavourable sign, but it must not be confused with the râles of bronchiectasis which may be present in the fibroid form of this stage. The differentiation of the two does not form part of our present subject. The localisation of the signs does not help us much in this stage, except in the respect that the more limited the area affected, naturally, the more favourable must be the prognosis. Again in this stage the influence of antecedent conditions in the prognosis need not be discussed. But one class of "individual symptoms" and complications becomes of the utmost importance. Dyspnœa, especially on exertion, but also during rest, is nearly always present and is unfavourable for prognosis. Yet its pathology and its influence on the prognosis differ in the two conditions of the stage. In the condition of cavitation the dyspnœa is due almost entirely to loss of lung tissue, and although in amonnt it is not usnally so great as in the condition of fibrosis, yet its prognosis is more unfavourable. In the condition of fibrosis some of the dyspnœa no doubt is due to loss of lung-substance, but its greater part (as I have elsewhere shown) is caused by non-expansion of the thorax over the affected areas. The expansion of the thorax is of great importance in the snoking of blood into the heart, and if interfered with the supply of venous blood to the lungs for aeration is lessened and dyspnœa must result. Bnt such a state is not

so dangerous as is great loss of lung tissue, and consequently while the dyspnœa is greater in the fibroid than in the cavernous state its prognosis is more favourable.

In the third stage the state of the circulation and with it that of the general body condition must be carefully watched, for heart-failure is one of the most serious complications. Any sign of its appearance, such as blueness and coldness of the extremities and weakness of the heart-sounds, should place the physician on his guard. Pneumothorax, again, is a formidable complication, and while principally occurring in the third stage, may at times be found in the second stage. But its danger is, I think, mostly limited to the moment of its occurrence. Then, certainly, it may cause death from shock. But when once the shock has been recovered from I do not consider the prognosis of pneumothorax in a tuberculous lung to be so unfavourable as has been so often thought. It scarcely requires treatment and often does well. Undoubtedly, like any other complication, it adds to the gravity of the condition, but lately I had four cases at one time among my in-patients at Brompton and all of them left the hospital free from pneumothorax and with their lung condition otherwise greatly improved. Pneumothorax is more common in cavitation than in fibrosis.

But hæmoptysis in this stage is a most serious matter, and its occurrence to any great amount must cause, to say the least, grave doubts of the patient's recovery. It is the greatest danger of this stage of the disease and is more frequent in the cavernous than in the fibroid state. As in the first and second stages it may be due to mere congestion or to ulceration of a vessel, but, if copious, it is most frequently caused by rupture of an aneurysm of the pulmonary artery in a cavity. I show you here what I think must be a unique collection of such aneurysms, occurring in almost every variety and with almost every form of surroundings. Their presence is a warning that percussion should always be very lightly employed, for a study of these specimens will convince you that the slightest jar of the thorax might be sufficient to cause rupture of the aneurysm. While I was pathologist at the Hospital for Consumption and Diseases of the Chest, Brompton, I only once failed to find such an aneurysm in a cavity after fatal hæmoptysis in the third stage. Observe, too, that the aneurysms are often found in only small cavities, so small as to be detected only with difficulty. The aneurysms are caused by suction. During cough the air contained in the cavity is partially expelled and the cavity walls are compressed, but on the relief of the pressure the walls expand once more and before the full quantity of air can gain re-admission there is a period of negative tension in the cavity which acts as a suction power on the wall of an exposed artery. Finally, it must be remembered that for a long time, for

many years in fact, tuberculous matter may remain embedded in the walls of an apparently healed cavity or in a mass of fibrous tissue, and though the disease is quiescent, yet at any time a fresh outbreak of the disease may occur. The patient, perhaps, need not be informed of this, for he can scarcely avoid it in any way than by the general attention to hygiene which he is bound otherwise to pay, but it should be remembered by the physician in formulating his prognosis.

I have not dealt with all the elements of prognosis, but only with those which seem to me to be of most importance. In my next lecture I will discuss with you a few points of treatment.

LECTURE III.

Delivered on Nov. 15th.

MR. PRESIDENT AND GENTLEMEN,—In the previous lectures I asked you to think of the tubercle bacillus in its progress, of how we can estimate its influence upon the lung tissue and the general system, the extent of its progress, and the likelihood of its further action. Now I come to the question of how we can prevent its action and progress and remedy the results of its action. Once more I ask you to think of pathology, for in a perfect knowledge of that must consist not only our prognosis, as heretofore discussed, but also our rational treatment. We must consider (*a*) how we can increase the resistance of the tissues (normally present) to the influence of the bacillus tuberculosis and its congeners; (*b*) how we can hinder the action of the bacillus by destroying its congeners, the staphylococcus pyogenes and the pneumococcus; (*c*) how we can hinder the action of the bacillus by interfering somewhat with its own vitality; and, finally, (*d*) what means can we adopt to kill the bacillus *in situ?*

(*a*) We can obtain increase of the resistance of the tissues by adding to their vital power and this can be done, and has been done since the disease was first known, by over-feeding, fresh air, and adjuvant measures. Before recent agitation we had been doing all this, and I show you here a record from my in-patient department at the Hospital for Consumption and Diseases of the Chest at Brompton of a case, treated on just simply the old lines of care, supervision, good feeding, and especially discipline of habits under a competent sister of the ward. The patient gained in weight 21 pounds in a fortnight, and he is not a very unusual example. Others show similar improvement and that without other treatment which need be considered. The "Open-air Treatment" is, of course, good as adding to the vitality of the patient and increasing the resistance of his tissues. We have practised this, more or less, not only in pulmonary tuberculosis but in other diseases also, long before it was brought before the public so prominently as has been done recently. Debove first advanced the idea of forced feeding. Many had recommended open-air in phthisis, and yet let us give honour to the men who systematised the methods. But, like all enthusiasts, they were, as I think, somewhat wrong. It is right to stimulate the absorptive powers and to encourage them to deal with cod-liver oil, maltine, excessive food, and so on. It is right to make the patient breathe pure air, cold

air (if needs be), and again to harden bimself to exposure—*if he can do so.* But I would like to give you a word of warning. The profession seems to have gone mad on this matter. Remember wbat Wilkie said about *his* methods. Someone asked him how he mixed his colours so as to get such wonderful effects and be replied, "Juist wi' brains." Mix your prescription of open-air treatment (so-called) with a little common-sense. Now, is it common-sense to make a patient sit down and try to eat another mutton cutlet when he has previously vomited two? Yet I am told that this bas been done in a well-known sanatorium and tbe patient commended for his perseverance. Surely his digestive organs required a little more consideration. And when we know a certain patient to he very liable to the effect of slight chills and also to inflammation as the result of such chills, is it necessary to put bim into the open air, covered as it may be from the external atmosphere, but inhaling the cold air into his bronchi, in order to "harden" him? We sometimes cry down the methods of the bone-setters, rightly or wrongly; but surely what I have described savours of them, and I say at once that this idea is wrong. You must mix the open-air treatment and also the treatment in sanatoria "wi' brains" or else leave them alone. But let it not be supposed that I cry down the open-air treatment. I have seen what good it may do with and without the discipline of a sanatorium. I have known what good may be got by it, in the best of circumstances, also in such open air as we can obtain in the Brompton Hospital, there, too, with discipline and good feeding; and I have known one patient (whom I saw with Dr. C. F. Knight) to do surprisingly well when dwelling in a tent erected in a back garden in Fulham. But we must remember that all these are only methods of bolstering up the tissues against the bacillary invasion.

Drugs of all kinds have the same effect. So, too, have other remedies which will be mentioned later, though their advocates may possibly take a different view of their action. I have used arsenic for many years as a hæmic stimulant in pulmonary tuberculosis and for the reason that, from some cause or other, iron is not well borne by phthisical patients. I have seen good come from its use and I refer to the matter here because of what has recently been said as to cacodylate of sodium being a cure for tuberculosis of the lungs. I have used it, and it is useful. It is a good alternative when arsenic by the mouth is not tolerated, and when one wishes to give the same or even an increased dose of the drug by the skin. I bave prescribed it in blood diseases and rarely with ill effect, hut it acts only as a stimulant to the formation of red blood corpuscles and therefore can only have a very indirect effect upon the tubercle bacillus. It is a useful tonic remedy, and that is all.

Under this beading there may be mentioned my colleague Dr. S. H. Habershon's treatment by tbe subcutaneous injection of glycogen and tbat of De Backer by the administration

of special preparations of yeast, though the consideration of the latter more properly belongs to a later section. Of these methods I have no personal knowledge and will say little. Dr. Habershon's idea is to increase the phagocytal power of the leucocytes by supplying them with glycogen as a stimulating food, and I hear from him that he has had some encouraging results. He has not yet completed his work but allows me to mention it here. De Backer holds the view that the yeast cells may act as additional phagocytes and absolutely destroy the tubercle bacillus. Allied to Dr. Habershon's method is that of subcutaneous injection of nuclein which will be more conveniently described below.

I cannot within the limits of the lectures discuss with you all the methods of treatment which have been adopted, and most of them discarded, in modern times. I wish to devote the remainder of this lecture to a description of a method of treatment of pulmonary tuberculosis and also of other disorders of the lungs which I have been working at for some time, which is on absolutely new lines, and which I have reason for saying is likely to be successful. I give it now to you for the first time in order that my professional brethren may form an opinion upon it. Its object is to fulfil the indications mentioned under the sections (*b*), (*c*), and (*d*). We would like to kill the tubercle bacilli *in situ* as mentioned in (*d*). But failing that, we may do good by weakening its action (*c*) and so enable the body powers to deal with it more advantageously, and finally, if we can produce no good action upon this very resistent tubercle bacillus directly, we may be able (*b*) to destroy the more vulnerable assistant germs, the staphylococcus and pneumococcus. What follows I must ask you to consider as a preliminary communication to which details will hereafter be added elsewhere, and I will style the subject

Asepsis of the Lung.

It appeared to me that the anatomy of the lung-circulation lent itself to a special mode of treatment. We have seen how successful, and at times unsuccessful, may be the effort to increase the vitality of the lung by excessive feeding, open-air, and so on. No pronounced effect is produced on the disease by inhalations of antiseptic vapours, for these cannot be administered so as to pass the glottis in any such strength as could produce effect upon germs, even if the inhalations ever reached the lungs. They do not reach the lungs, for we have reason to believe that they never go much beyond the bifurcation of the bronchi in any appreciable strength. We know only too well, however we may appreciate our successes, that by all these methods we have a lamentable number of failures. The same, I am afraid, must be said of many other methods of treatment which have been put forward at various times and this view I mention with every due respect to the authors of those

methods and to the immense amount of work which they have given to the subject. Undouhtedly the rational cure for pulmonary, as for all tuherculosis, is the administration of au antitoxin derived from the tubercle hacillus itself, as was designed hy Koch. But, as you are well aware, this has hitherto proved useless and worse than useless. So we must still say of the further attempts in the same line by modifications of nis methods. Some day, though probahly not in our time, the end thus aimed at will be attained and then we shall have a perfect cure. But before this result is reached we mnst still go on treating our patients and trying to cure them. Again, attempts have been made to ohtain an antitoxin from the growth of the tubercle bacillus, not on our lahoratory cultivations, as was done by Koch, but in the living hodies of such animals as the ox, the ass, and the horse. I allude here to the so-called anti-tuberculous serums, all of which have proved to be practically useless. It has appeared to me at times that, seeing how tuberculous patients who suffer from pleural effusion seem to be much better when the effusion is allowed to be absorbed naturally and is untreated by paracentesis—and this yon will remember I alluded to in my former lecture—that the good result might he due to the re-absorption of an anti-tnberculous serum grown on human soil. It is not easy to get such serum without doing an injustice to the patient, for, as I have stated, the effusion is best left alone. Yet occasionally it happens that an effusion is so great as to by its actual presence endanger the life of the patient. Such a case occurred to me a little time ago at St. Mary's Hospital and I determined, on removing the effusion, to ascertain whether it possessed any property which was antitoxic to the bacillus. But hefore nsing such a sernm for experiment it is absolutely necessary to remove from it all active tubercle bacilli, and I could not conceive of any other method of doing this than by passing it through a Pastenr's filter under pressure. But the solution could not by any meaus he made to pass through the filter and so the experiment had to he ahandoned. Possibly another chance of which I can take advantage may offer itself in the future. (It may be interesting to record the later history of this case in connexion with the danger from hæmorrhage to which the patient is liahle in the third stage and to which I referred at the close of my last lecture. The patient, a youth, aged 18 years, was taken into the hospital because of his effusion and I aspirated his chest though I knew that he had phthisis in the third stage. After a few days he had recovered from his effusion and his phthisis heiug qniescent I allowed him to leave. He walked from the hospital down Praed-street, was overtaken hy copious hæmoptysis before reaching the Great Western station, and was brought hack to the hospital dead. I was very thankful that his hæmoptysis did not occur during my aspiration.)

I have mentioned the methods of Dr. Habershon and De

Backer by which it has been thought possible to inject underneath the skin substances which may reinforce the lung tissue in its fight against the bacillus—namely, glycogen and yeast respectively. Dr. Habershon's work is not yet completed, and I am afraid that De Backer's results must he said to be unsatisfactory. Others, too, have attempted to administer antiseptics by means of the skin—that is, subcutaneously—and without any success. Nor is this to be wondered at when we think that any remedy placed under the skin must be diluted with all the fluids of the hody before it reaches the lungs and then cannot fail to be powerless. For many years antiseptics, like creasote and its essence guaiacol, have been given by this method in so dilute a form, to begin with, as to be useless even if applied directly to the bacillus. Yet they are still further diluted in the stomach and more or less altered in their passage through the liver and other digestive organs as to have not the slightest effect for our purpose when they reach the lungs. It is true that by reason of direct absorption through the blood-vessels of the stomach these drugs—especially creasote, guaiacol, iodoform, and naphthalene, all of which I have used—reach the lung unaltered and can be detected in the expired air. It is true also that these expired vapours are of some slight use in preventing the decomposition of the secreta in the lung. All of these points I have observed and willingly admit. But they have not the faintest direct effect upon the progress of pulmonary tuberculosis; in fact, they are almost useless. It has again been suggested hy the followers of De Backer that the yeast-cells, and again other reagents, should be injected directly into the infected parts of the lung; and once more I admit that good results have ensued. But remember, however, that such injections cannot reach very far into the tissues, and they must be very numerous, therefore painful and frequently repeated, if they are to touch even the recognised foci of disease. But what about the unrecognised foci? For surely none of us, however experienced, will venture to say that he can detect by physical examination every spot of the lung affected by an attack of tuberculosis. And what about the patches which, recognised or suspected, are beyond the reach of any injection syringe? Surely there will always remain such spots, inaccessible to all such treatment and ready to spread to neighbouring and other parts of the lung. Such treatment cannot possibly be really curative. And as to the more surgical procedure of removing affected parts of the lung—and this has been done—well, the less said the better, for fear that the mere mention of it may encourage an unduly bold surgeon to practise it.

But let us come back to what I have mentioned above—that the anatomy of the lung-circulation lends itself to our treatment. This has been impressed upon me for some time, for it must be obvious that anything introduced into the veins must necessarily pass directly through the lungs by

way of the right side of the heart and without dilution with other fluids of the body than the amount of blood contained in the right ventricle at the time when the injected fluid reaches that cavity. I determined to try this method, and with much trepidation when I thought of the manifest dangers involved in the introduction of a foreign substance into the blood-stream. But I was encouraged to pursue the investigation by hearing that my colleague, Mr. Ernest Lane, had been treating syphilis by injecting 2 per cent. solution of cyanide of mercury into the veins and by seeing the beneficial effects upon one patient of mine at St. Mary's Hospital whom he treated for virulent syphilis. I went to the Lock Hospital to see Mr. Lane's method, and seeing what he had done I thought that if he could inject cyanide of mercury with impunity—for he had done it some 3000 times without other mishap than the occasional missing of the vein by the needle—and seeing, too, that cyanide of mercury was not only anti-syphilitic, but also a powerful germicide, I also might safely use the same on tuberculous patients. Mr. Lane was in the habit of injecting 20 minims of a 2 per cent. solution, but I injected 30 minims of the same solution into the veins of two patients at the Brompton Hospital. But as that strength would be useless for my purpose, and wishing to use the drug in stronger solution, I asked my colleague, Mr. Plimmer, to inject a solution of 5 per cent. into the ear-vein of the rabbit. The rabbit died before the injection could be completed, and, as we found, from coagulation of blood in the right side of the heart. I immediately hurried, as you may readily understand, to see what had been the effect of the weaker injection upon my tuberculous patients and found that both of them had become very collapsed and had suffered from painless diarrhœal flux. It was obvious that what might be safe enough for Mr. Lane's otherwise strong men suffering only from syphilis would not do for my weakly tuberculous patients. Moreover, it seemed probable, though I offer this only as a suggestion, that the mercury of the cyanide combined with the albumin of the blood, causing coagulation, liberating cyanogen, and the latter, combining with water, produced a considerable amount of hydrocyanic acid, the effects of which would be to cause vaso-motor collapse and the diarrhœa which was observed.

Let me here say that before using any other remedies and those in any particular strength I was always careful before applying them to patients to test their safety upon rabbits—or later on myself. Rabbits and monkeys are the only animals, except man, which offer suitable subjects for such trials, since their superficial veins can be easily reached without incision of the skin. Obviously, if the intravenous method is to be practised frequently, as it must be for therapeutic purposes, section of the skin by the knife is out of the question, and, indeed, I would incidentally commend to the surgeons the results of

technique which I have arrived at in various ways, as being improvements upon the methods hitherto adopted for intravenous injection when employed for other purposes. Again, let me remark that all these trials upon animals were performed by Mr. Plimmer who possesses—as I do not—the requisite legal permit. Rabbits were used as being cheaper and more easily obtainable than monkeys. Further, before any advance of method was attempted, we tried to inject about 10 cubic centimetres into the ear-vein of a rabbit, that is, five times the quantity I wished at that time to inject into a man, and weight for weight an enormous dose. This having been done with safety I concluded that I was justified in applying the method to man.

To conclude this part of the subject I must here refer to an objection which may possibly be raised in reference to experiments upon animals. It may be asked, Why did I limit myself to merely testing the safety of the various solutions to be mentioned and did not first produce tuberculosis of lungs in the animals and attempt its cure by injection? Here are my reasons. Rabbits and monkeys were the only animals available for this particular purpose and they are very liable to tuberculosis. But it is by no means so easy as you would otherwise suppose to artificially give them tuberculosis of the lungs with certainty. Tuberculosis of any other organ would be of no use for my purpose, for it is only the lungs which are supplied directly with blood from the external venous circulation. Now it is possible to infect a rabbit's lungs with tuberculosis by injecting an emulsion of a culture of tubercle bacillus into the ear-vein. Mr. Plimmer has occasionally done this but never with certainty. The emulsion is prone to coagulate and block the vein and it is very difficult to determine whether a given culture is toxic or not at the moment of injection. I tried to get tuberculous monkeys from the Zoological Gardens, wishing to attempt to cure them; this would, I think, be an experiment permissible by the law. But the authorities of the Gardens, who were most courteous to me, naturally did not wish to part with their monkeys until they were practically moribund and useless for any therapeutic effort. Rabbits can be made to suffer from tuberculosis of the lungs by subjecting them to the inhalation of dust containing tubercle bacilli, as has been shown by Cornet. But such infection cannot be done without some risk to other persons than the experimenter. For instance, Cornet himself, when he entered the room in which the rabbits lived, in order to stir up the dust, and in spite of taking such precautions as plugging his nostrils with cotton wool, nevertheless found afterwards tubercle bacilli in the mucous secretion of his nose. Further, such a series of results as could be obtained in this way would require an almost endless time and far more continuous observation than I could possibly give to them. But, of still more importance to a practising

physician, there seemed this objection, that the animals could not tell one how they felt and in human beings we have to consider not only pathological anatomy but many other points in the well-being or ill-being which cannot easily be ascertained from animals. Therefore, I contented myself with ascertaining the safety of such remedies as I wished to apply—from observation on animals and myself—trusting for further results to actual trials upon patients.

Having failed, then, with the cyanide of mercury I cast about for some other germicide. Perchloride of mercury, carbolic acid, and other well-known antiseptics would obviously be useless because of their destructive action upon the blood. I tried, however, upon a rabbit the effect of the potassic iodide of mercury in the way described, for this salt is said not to cause coagulation of the blood. The result, however, was that the rabbit died in about an hour, not from intravascular coagulation like the former one, but from simple poisoning and stupor. Thus far the trials for an intravenous germicide seemed to be futile. I heard, however, from Mr. Wallas, the pharmacist, that diastase had been found to digest cellulose. Now it has been observed that the tubercle bacillus contains grains of cellulose[1] and it is probable that its envelope consists of some form of cellulose. From rough experiments which I made it seemed that diastase had really some power of destroying the tubercle bacillus as it exists in the sputum. This was almost a forlorn hope, but I determined to try the effect of a solution of diastase used intravenously. It was by no means easy to do, for diastase forms a very mucilaginous solution, totally unfit for such injection. Ordinary diastase I found to be quite useless, but it is possible to get a solution of taka-diastase of 5 per cent.—that is, the product known by that name and discovered by Takamine by growth of germs upon bran. The substance has some undetermined composition, it is certainly mucilaginous, and has a diastasic power. It is of great use, as probably you know, in the treatment of flatulent dyspepsia by helping to digest the starches. It forms with water a thin mucilage which after standing for awhile deposits something which looks like a colloid form of some crystalline substance. After a while, however, a brown translucent fluid is obtained lying over the deposit; this is stable for a few hours, and undoubtedly possesses diastasic properties. But before using this as an intravenous injection it was above all things necessary to make the solution sterile of germs. For this purpose heat could not be employed, for it would destroy the diastasic ferment. The solution was too unstable and too mucilaginous to pass through a Pasteur's clay filter, and, besides, this process would require to be repeated immediately before each injection, which would be impracticable

[1] See Lehmann, Bakteriologie.

in clinical use. I tried the addition to the solution of snch a small amonnt of perchloride of mercury as wonld probably act as a germicide. This precipitated the diastase in a few hours, but adding it shortly before the injection I managed to get a solution which would keep for a short time in the fluid condition and this I tried, without ill effect, npon rabbits. Later, Messrs. Squire and Sons prepared for me a fairly permanent solntion of taka-diastase made with tri-cresol as the antiseptic, and afterwards with formic aldehyde in the strength of 1 in 250,000. This I tried npon patients with the view of therapensis which I have mentioned. I injected 30 minims—that is, two cubic centimetres—at intervals of fonr days. But the immediate result of the injection (a result which appeared in abont half an honr afterwards) was rigor, pyrexia, and sweating; in fact, an exact imitation of an ague attack. The pyrexia reached to the height of about 102° or 103° F. and afterwards the patients felt much better; certainly they took food more freely and there could be no donbt of some improvement in the condition both generally and as jndged by the physical signs of the chest. Yet there was not so great an improvement as to encourage me to pursne the treatment. Mr. Horace Brown, F.R.S., so well known for his researches on diastasic zymes, very kindly gave me his advice on the question under discnssion and suggested that I shonld try the effect of cytase, snch as he had obtained from freshly crnshed oats. He has shown, and has described in his published papers, that this snbstance is very powerfnl in digesting the cellulose envelope of cereals. I show yon here a solution of cytase which has been prepared for me by Mr. Peter Squire in a form which might be used for intravenous injection, and the solution I have found to have a very definite solvent action even upon cotton-wool. Again, you see under the microscope two sections of barley. One has been treated with a solution of formic aldehyde alone—that is, with an antiseptic; the other with the same reagent, but also with cytase, and the latter specimen shows a marked solution of the cellulose envelope of the grain, while the former appears to be intact. We would like to get the same solution of the tnbercle bacillus in the lung, but, unfortunately, the reaction is very slow and is likely to be greatly interfered with by dilution in the process of intravenous injection. I have obtained the solution of cytase which I show you only within the last few days. I will certainly try its effects, for possibly one may be able to hasten its action.

In the last lecture I mentioned the snrprising effects which I had obtained by administering nuclein by the mouth in the treatment of such tuberculous glands as conld not be removed by operation. I tried nuclein given thus, npon patients suffering from tnbercnlosis of the lnngs, and without the slightest effect. The idea, of conrse, is that the nuclein will so strengthen the leucocytes as better to enable

them to fight the bacillus. But it seemed to me desirable to ascertain what effect the same substance might have when used intravenously. For this purpose I employed the Liquor Nucleinicus of Messrs. Squire and Sons, a sterilised solution of the nucleinate of soda (which I show you), and I injected two cubic centimetres on each occasion. The results were exactly the same as in the case of the diastase solution, a distinct febrile reaction and afterwards some improvement in the condition of the patient but the results were not encouraging, nor do I think it desirable to use a remedy on a tuberculous patient which, like diastase, nuclein, or the tuberculin of Koch, increases, if only for a time, the already existent pyrexia. Yet I think this matter may very well be a subject for future investigation.

The pyrexial reaction after the use of such prospective remedies is very curious and interesting. I may say here, with Dr. Habershon's permission, that in his experiments on the subcutaneous injection of glycogen, he found that the same febrile reaction occurred when the glycogen employed was not entirely freed from nitrogenous matter and did not appear when this matter had been previously removed. Again, during the last few months I have treated four cases of aneurysm of the aorta by the intramuscular injection of sterilised solutions of gelatin, following, with some little modifications, Lanceraux's method. After each injection I observed a distinct febrile reaction, the temperature on one occasion rising to 104° F., but always (in these cases) without any inconvenience to the patient. Putting all the results together, one is led to the idea that the fever is dependent upon the introduction into the system, by any method whatever, of some foreign albumin.

But in the course of the above-mentioned experiments the question of antisepsis became, as I have hinted, very important, and I thought that one ought to ascertain whether the results had been produced by the diastase or the nuclein or by the antiseptic used to sterilise the solutions. Mr. Squire told me that he found 1 in 250,000 of formic aldehyde a sufficient antiseptic and this, and afterwards 1 in 100,000, I tried on rabbits and afterwards on patients. I need not give you further details, but let it suffice to say that I at last reached a solution of 1 in 2000 of the pure formic aldehyde gas, that is, 1200 times stronger than I had at first used. In my earlier trials I found that I could inject two cubic centimetres of solution in the space of five heart beats, but by later improvements in the technique I could admit into the veins at least one cubic centimetre for each heart beat and frequently double or treble this proportion if the patient could be kept quiet. The reason for measuring the rapidity of injection by heart beats and not by seconds you will see in a few moments. We can calculate with fair accuracy what is the strength of such a germicide solution passing through the lungs when injected into the veins. Using for the purpose of injection

the syringe ordinarily employed with anti-tetanic sernm, I at first fonnd, as I have mentioned, that I could inject two cnbic centimetres in the average course of five heart beats, meaning that two-fifths (or 0·4) of a cubic centimetre were injected with each heart beat and therefore mingled with each one filling of the right ventricle. The right ventricle of a man who weighs about 10st. 7lb. is believed to hold approximately 100 cuhic centimetres, the solntion used is of a strength of 1 in 2000, therefore the strength of the solution in the right ventricle will he $\frac{2}{5} \times \frac{1}{100} \times \frac{1}{2000} =$ 1 in 500,000. Not a great strength, it is trne, but probably of some efficacy seeing that a certain amonnt of the reagent will remain in the lnng to he added to hy future heart heats. Moreover, as I will shortly show yon, it is possible by other methods to inject qnite easily one cnhic centimetre for each heart beat and even twice or thrice that amount. But with the one cubic centimetre for each heart heat we reach a strength in the right ventricle of 1 in 200,000, which is of formic aldehyde a strength which has been proved to he a very efficient germicide. To anticipate, I may say that I have been able to inject 50 cuhic centimetres in the space of 25 seconds, when the pulse was heating at only 60 per minute, and even this rate of injection may at times be exceeded. But this speed means two cubic centimetres for each heart beat of a 1 in 2000 solution of formic aldehyde which is added to each filling of the right ventricle, making a solution of 1 in 100,000, which will sluice out the lung for the space of about 30 heart beats. This certainly must he a fairly powerful germicide even for the tubercle bacillns, let alone its more easily attackahle congeners, the staphylococcus pyogenes and the pneumococcus. Therefore I determined to use such a solution in the treatment of pulmonary tuherculosis. At first I did not venture to inject more than two cuhic centimetres at one time, hut hecoming holder I increased the quantity and at the same time the strength of the solution until, hy means of the syringe nsed for diphtheritic antitoxin, I could inject 10 cubic centimetres of a 1 in 2000 solntion of pure formic aldehyde gas at one time. Wishing to go still farther I thought it desirable to make the solution of the gas, not with plain water, hnt with normal saline solution so as to prevent any destruction of the red corpuscles, and it is this solution which I show you now, as prepared by Messrs. Squire and Sons, hy their own methods of sterilisation, and called for convenience "Hæmasepsin."

It will be convenient now to describe the method of injection. It seems an easy thing to pierce a vein with a needle and to inject a solution into its interior. In practice it is anything hut easy to do so. The vein rolls under the needle and presents great resistance to the piercing. Again, the needle, in spite of all care, will often transfix the vein or at least puncture the opposite wall. In either case not only does the injection fail hut the solution is de-

posited in the circumvenous tissue and causes great pain. It is only after considerable experience and with a certain amount of technical skill that the injection can be properly given, and in view of the manifest dangers no one should lightly undertake it. I find it best first to ligature the arm above the elbow so as to make the veins prominent, and then plunge the needle boldly into one of the large veins on the front of the elbow. The ligature of the arm should now be loosened and the injection proceeded with, carefully watching for any swelling which would indicate escape of the fluid into the circumvenous tissue. I have tried to use a needle on the principle of the Southey's trocar, hoping that on the withdrawal of the point one might easily introduce the canula farther into the vein without risk of re-piercing the wall. This, however, I have not found feasible. Again, I have tried what one might call a valvular puncture—viz., perforating the skin first and afterwards piercing the vein at a higher point. This is difficult to do because of the rolling of the vein—and it must be remembered that any attempt to steady the vein leads to its collapse—and, moreover, there is considerable risk of causing a troublesome hæmatoma in the subcutaneous tissue. For these reasons it is best, I find, to plunge boldly into the vein through the skin, first anointing the skin with carbolic vaseline, 1 in 12. Naturally the needle and the skin must be rendered perfectly aseptic and if the patient be very nervous the skin may be sprayed with a solution of cocaine to anæsthetise it, though this is really unnecessary.

So far, however, the limit of an ordinary syringe—10 cubic centimetres—was reached, and to give larger amounts with one puncture required special apparatus. I therefore devised and had made for me by Messrs. Squire and Sons a syringe (Fig. 1). It is really a miniature stomach pump the tube of which holds a few cubic centimetres and can be replenished from the bottle without removing the needle from the vein. But this instrument must be used with the greatest care, since the mere movement of turning the stop-cock and reversing the piston is frequently just enough to cause the needle to transfix the vein and ruin the injection. Because of this I have employed mere hydrostatic pressure, using an ordinary 100 cubic centimetre burette of narrow calibre, so as to get as high a head of fluid as possible, and I connected this by an indiarubber tube with a rather wide-bore needle. The burette is furnished with a stop-cock, and the needle being rendered aseptic a certain amount of fluid is run through it so as to fill the whole apparatus with the reagent. I may say here, however, that no fear need be entertained from the entrance of a small amount of air into the veins. This is an old-fashioned surgical fallacy. For ordinary use the burette is the more convenient instrument, though somewhat cumbersome to carry, but occasionally it happens that the venous pressure is so great that

the syringe is useful. It was by means of the simple burette and of a large bore needle that I was able to inject one cubic centimetre of the hæmasepsin during each heart beat. Later, however, I have used in addition to the burette the

FIG. 1.

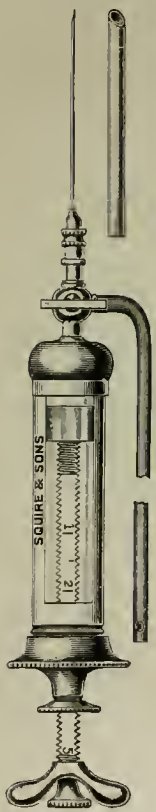
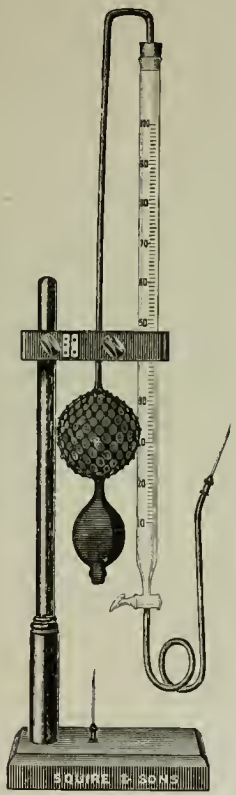


FIG. 2.



hand-pump you see here, which enables one to make a much more rapid injection (Fig 2). After the injection the needle is withdrawn. A little bleeding may occur and it may sometimes be necessary to cover the puncture with a few

tbreads of alembroth wool and collodion, but commonly the pressnre of the finger upon the puncture for a moment or two is enongh to stop all oozing. The part is triflingly tender on the next day, bnt no fnrther ill-effect is nsnally seen. The slow injection of the solution at ordinary room temperatnre is accompanied by a curions cramp-like pain in the fingers and np the arm as far as the axilla. This I have observed on myself. The pain can be prevented by waiming the solntion to blood-heat, but I have grave doubte whether this is desirable. The heating may possibly be done with due precantions witbont destroying tbe effect of the remedy, but it must be remembered that formic aldehyde is a very volatile substance and the heating of its solution may cause the gas to be driven away. Tbe pain is not great and can really be very easily borne up to the injection of 50 cubic centimetres, so I think it better to give the solution cold; moreover, rapidity of injection almost minimises the pain. In this way by one or other instrument I succeeded in giving daily injections of 50 cubic centimetres without any bad or unduly unpleasant effect. This means, as stated above, tbat for at least 50 heart beats the lnng was slniced out with a solution of formic aldehyde of a strengtb of 1 in 200,000 or more. The stronger the solntion and the more prolonged its contact witb the lung tissue, the more powerful would be its action as a noxious agent on the germs contained in the lung. It was therefore desirable to ascertain tbe danger-limit of snch injection. This could not be found by experiments npon animals—it was scarcely fair to submit a patient to the risk—so I bad the trial made upon myself. One morning at about 11 o'clock I asked my house physician, Dr. van Praagh, to inject 100 cubic centimetres of a 1 in 2000 solution of formic aldehyde into a vein of my arm. I wished to ascertain whether tbe aldehyde passed out of the kidneys as such, and in about an hour it was detected in the urine by tbe rosanilin test. Incidentally, however, it appeared that albnmin was present, but no blood-colouring matter, and tbat tbe urine was very acid. Now, at that time of the day the urine of an ordinary man is usually alkaline, and my own is generally so alkaline—as I have frequently observed—as to deposit pbosphates at the time of micturition. The ascertained acidity of the nrine was therefore abnormal and was probably due to the presence of formic acid, though I had no means at hand for testing tbis. In about another honr, all these conditions had disappeared. A few days later Dr. van Praagh injected into my arm, and at a somewhat qnick rate, 263 cnbic centimetres of a 1 in 2000 solution. We only stopped the injection because our stock of solution was exhansted, thongh I certainly experienced a good deal of cramp-like pain in the arm and a curious nervous nneasiness in the thorax and especially in the cardiac area. Immediately I passed nrine whicb was copiously loaded with blood. Many red corpuscles were fonnd in tbe urine, but not so many as wonld be expected from the amount of blood-

colouring matter present. An hour later the urine was still more bloody. Then for about four hours it happened to be inconvenient for me to micturate, but on doing so it was obvious that the blood had formed small clots in the bladder, which were expelled only with some straining, and for some little time there was considerable irritation of the bladder. Still later the urine was of a brownish tint containing no ordinary albumin or ordinary blood-colouring matter, but I had no means at hand to collect it or to further ascertain its composition. On the next day all urinary changes had disappeared, but I was very dusky and yellowish as regards the sub-conjunctival tissue. During this period, too, I had a certain amount of bronchial catarrh and was conscious too of being unduly irritable in temper. It was here a question as to whether the bad results were due to the formic aldehyde or to the volume of fluid injected, so four days later I determined to have injected a solution of 1 in 1000. This is really (as I found afterwards) a caustic solution and I could not bear the injection of more than 63 cubic centimetres. The injection was stopped because of the extreme cramp-like pain and faintness. Very shortly afterwards I suffered from severe bronchial catarrh, accompanied by much wheezing in the chest and the expectoration of considerable quantities of frothy, white mucus. Soon (but subsequently) there occurred catarrh of nearly all the mucous membranes, except, as far as one could ascertain, that of the stomach. There was much running from the nose and conjunctivæ, there was great irritability of the bladder, but no urinary change, and a mild but troublesome dysentery, the bowel pouring forth much clear mucus. On the next morning, too, there was a thrombus in the injected vein of about three inches in length, surrounded by an inflammatory zone and very painful. The thrombus has now become smaller and less painful, but it has not entirely disappeared. This was an unpleasant experience, but it served its purpose and showed that the maximum strength of solution to be employed in its then form must not exceed 1 in 2000 and the maximum injection must not be more than 50 cubic centimetres for an adult.

The experiments showed more. They are imperfect scientifically, for I was not prepared for the result and had not means at hand for its proper investigation. They are sufficient, however, for therapeutic purposes, and naturally I do not care to repeat them on my own person. They show that formic aldehyde is an irritant to the mucous membrane of the lungs and that even after passing through the lungs, its solution may be of sufficient strength to irritate the mucous membranes connected by circulation with the left side of the heart. I have already mentioned what strength of solution we may expect in the right side of the heart from the injection into the veins of a 1 in 2000 solution of formic aldehyde. Naturally this will be

enormonsly diluted hy the time it reaches the general circulation and it is difficult to estimate this dilution. But let it he remembered that a dilution insufficient to kill the tnhercle hacillns may nevertheless weaken its action, and may still kill other minor germs, snch as the staphylococcus pyogenes or the pnenmococcus, the presence of which favours the growth of the tnhercle hacillus. Experiments are in progress to ascertain the effect of various weak solutions of formic aldehyde on the growth and action of these germs; the results of snch experiments I will puhlish later. Again, let me call attention to the fact that the aldehyde in strong solution caused bronchial catarrh. Below I shall have to mention that cough is not only unrelieved hut often increased dnring the treatment of patients hy this method. Possibly such mild irritation may he heneficial as a connter-irritant to the lung tissne, stimnlating it to more healthy action, hut its existence warns one that the treatment must he pursued with cantion and frequent inspection. In fact, I have sometimes found, as I will describe, that improvement only appeared when the treatment had heen suspended for a few days.

Again, to prevent disappointment, one ought to remember that the pulmonary artery—the only vessel directly affected hy the intravenous injection—is not the only artery which goes to the lnngs. As I have elsewhere explained it is the "fnnctional" vessel of the lungs, while the hronchial arteries coming from the aorta are the "nntrient" vessels of the lungs and are not primarily touched hy the injection. Nevertheless. I have not fonnd great need for snch warning in practice, so great is the diffusion through the pulmonary capillaries.

In estimating the result of such a method of treatment upon the hnman snhject it is of all importance to take care not to deceive oneself. Of, say, 100 cases of early tuherculosis of the lungs prohahly 90 will show good results with no other treatment than improved hygiene and feeding. If any new treatment were applied to such cases one could easily be persnaded that it was snccessful. Naturally one wonld always wish to carry on a treatment in an early stage, hut judgment of the effect of such treatment would he futile. For this reason I have only tested the treatment on severe and even desperate cases, thinking it hetter to meet with some failures if only one could get good resnlts in a few cases where other remedies might have prohahly heen useless. I append a few of such results, to he followed hy a further series shortly. The test points are the steadying and redncton of hectic temperature, the qnieting of the circulation, the diminution of the amount of spntum, the disappearance therefrom of pus and of the tnhercle hacillus and other germs, and the aholition of such physical signs as indicate active tuherculons mischief.

I will tell you, here, the method which I have pursued in testing for such results. In hospital and elsewhere I have treated thus some 50 persons. Some of them were at the Brompton Hospital with surroundings, feeding, and discipline specially designed for their complaint. Others were treated at St. Mary's Hospital with the ordinary course of dietary, &c., pursued in a general hospital. And not all of these had the intensive treatment which of late I have adopted. Dr. R. G. Reid of Lambeth has in consultation with me treated some 20 patients who might he considered equivalent to those at the Brompton Hospital, hut with their own home surroundings. Dr. A. Findlater of Edgware, who is in charge of the Hendon Workhouse Infirmary, has similarly treated seven cases with practically home surroundings, hut also in a country atmosphere, or as near that as one could obtain within easy reach of supervision from London. I must not here give you details of these cases hut merely the summary of the results. Almost every case has shown some improvement and in some this has been very marked. Most usually in my own cases the physical signs have diminished in amount as the earliest indication of improvement; appetite and general condition have heen hetter after injection, and in nearly every case the patient has gained weight. The sputum hecame more frothy and less purulent, and in a few cases tuhercle hacilli and other germs have already disappeared. I show you here one such patient. He came under my charge at St. Mary's Hospital in the autumn suffering from a very marked outhreak of the multiple pleuritic form of tuherculosis. His temperature, as you see, showed a rapid decrease, his physical signs diminished, tuhercle hacilli disappeared from his sputum, and now he seems to be perfectly well. If you will examine his chest you will find nothing hut some thickening of pleura in patches on the left side. Dr. Reid's cases have shown similar results in spite of the somewhat hard circumstauces under which the patients were placed. Dr. Findlater, who is here to night, will tell you himself of his results, one in particular heing extraordinary.

The patients should he carefully watched during the treatment, for you have heard how I myself suffered from the effects of an overdose of the injection. If the injection he pursued too long the formic aldehyde will unduly irritate the lung tissue and increase the symptoms. It is only practice and experience which can tell one when to suspend the treatment, hut, as a general rule, I should think it desirable to give up the injections for a few days when the temperature has fallen, when the sputum has become mucous and frothy, and when the cough is unduly trouhlesome. With regard to the latter symptom I do not see the same objection to treating it by opium as obtains in ordinary coughs. This cough is due to irritation of the pulmonary

mucous membrane, and the same irritation causes the excessive secretion of mucus. An opiate will relieve both and is not, I think, counter-indicated.

Though it is somewhat outside our present subject, I may here mention the results of the treatment on bronchiectasis. As you know, scarcely anything can have a fouler smell than the sputum from this complaint, and at times so bad is this symptom as to incapacitate the patient from intercourse with his fellows. A patient came under my care at Brompton who had been supposed to be suffering from this, though I found that he really had a tuberculous cavity of the base of the lung with pleural adhesions, which kept the walls of the cavity constantly stretched. This was a similitude of bronchiectasis. His sputum was very offensive, so much so as to render it undesirable to keep him in the same ward with other patients. It separated on standing into the three usual layers. At this time I had not given a greater injection than two cubic centimetres and that by the syringe. After even the first injection distinct improvement was observed in the condition of the sputum. It became almost devoid of odour, less purulent, and much less copious. He left the hospital much improved. I have treated a few typical cases of bronchiectasis similarly and with like, though not such immediate, results. But my last case requires special mention. My colleague, Dr. Percy Kidd, asked me to apply the method to one of his patients at the Brompton Hospital. The patient was a country policeman whose bronchiectasis and accompanying condition were so bad that he had been warned to leave the force if he could not get better. He was really unfit to associate with his fellow men. He had been treated by inhalations in our "guaiacol room," but when I saw him he was in a wretched condition, although he had showed some slight improvement. At this time he was coughing up much more than a pint per day of very foul sputum. I began with the two cubic centimetres of injection on each day and afterwards administered 50 cubic centimetres of injection by means of the burette. He rapidly improved and when I last saw him he was expectorating only three ounces of matter which had only a faint odour. He then had to leave the hospital in order to report himself so as not to lose his pension, but I have little doubt that he could have been permanently cured.

[Since delivering the lectures I have tried, by modifying the vehicle, to use a greater strength of the formic aldehyde solution. At present I will not give details, but I think the result can be accomplished. I purpose bringing the whole matter before one of our societies at an early date in order that it may be adequately discussed.]

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